CLAIMS

We claim:

A pharmaceutical composition comprising:
 a pharmaceutically acceptable carrier, adjuvant or vehicle; and
 a therapeutically effective amount of a compound having the structure:

$$\begin{array}{c|c}
R_{8} & Y_{1} & Y_{2} & Q \\
R_{1} & X_{1} & R_{2} & R_{3} \\
R_{2} & R_{3} & R_{4} & R_{5}
\end{array}$$
(I)

or pharmaceutically acceptable salt thereof;

wherein R_1 and R_2 are each independently hydrogen, halogen, -CN, -S(O)₁. $_2R^{1A}$, -NO₂, -COR^{1A}, -CO₂R^{1A}, -NR^{1A}C(=O)R^{1B}, -NR^{1A}C(=O)OR^{1B}, -CONR^{1A}R^{1B}, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or – WR^{1A}; wherein W is independently -O-, -S- or -NR^{1C}-, wherein each occurrence of R^{1A} , R^{1B} and R^{1C} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_1 and R_2 , taken together with the carbon atoms to which they are attached, form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

R₃ is hydrogen, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or a prodrug moiety or an oxygen protecting group;

R₄ is halogen, -OR^{4A}, -OC(=O)R^{4A} or -NR^{4A}R^{4B}; wherein R^{4A} and R^{4B} are independently hydrogen, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; a prodrug moiety, a nitrogen protecting group or an oxygen protecting group; or R^{4A} and R^{4B}, taken together with the nitrogen atom to which they are attached, form a heterocyclic or heteroaryl moiety;

R₅ is hydrogen, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

 R_6 is hydrogen, halogen, -CN, -S(O)₁₋₂R^{6A}, -NO₂, -COR^{6A}, -CO₂R^{6A}, -NR^{6A}C(=O)R^{6B}, -NR^{6A}C(=O)OR^{6B}, -CONR^{6A}R^{6B}, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or -WR^{6A}; wherein W is independently -O-, -S- or -NR^{6C}-, wherein each occurrence of R^{6A}, R^{6B} and R^{6C} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_6 and R_c , taken together with the carbon atoms to which they are attached, form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

 \mathbb{R}_a and each occurrence of \mathbb{R}_b are independently hydrogen, halogen, -CN, -S(O)₁₋₂R^{a1}, -NO₂, -COR^{a1}, -CO₂R^{a1}, -NR^{a1}C(=O)R^{a2}, -NR^{a1}C(=O)OR^{a2}, -CONR^{a1}R^{a2}, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or -WR^{a1}; wherein W is independently -O-, -S- or -NR^{a3}-, wherein each occurrence of R^{a1}, R^{a2} and R^{a3} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_a and the adjacent occurrence of R_b, taken together with the carbon atoms to which they are attached, form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

 R_c is hydrogen, halogen, -CN, -S(O)₁₋₂R^{c1}, -NO₂, -COR^{c1}, -CO₂R^{c1}, -NR^{c1}C(=O)R^{c2}, -NR^{c1}C(=O)OR^{c2}, -CONR^{c1}R^{c2}; an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or -WR^{c1}; wherein W is independently -O-, -S- or -NR^{c3}-, wherein each occurrence of R^{c1}, R^{c2} and R^{c3} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_c and R₆, taken together with the carbon atoms to which they are attached, form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

n is an integer from 1 to 5;

 X_1 is O, S, NR^{X_1} or $CR^{X_1}R^{X_2}$; wherein R^{X_1} and R^{X_2} are independently hydrogen, halogen, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or a nitrogen protecting group;

Q is hydrogen, halogen, -CN, -S(O)₁₋₂R^{Q1}, -NO₂, -COR^{Q1}, -CO₂R^{Q1}, -NR^{Q1}C(=O)R^{Q2}, -NR^{Q1}C(=O)OR^{Q2}, -CONR^{Q1}R^{Q2}, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or -WR^{Q1}; wherein W is independently -O-, -S- or -NR^{Q3}-, wherein each occurrence of R^{Q1}, R^{Q2} and R^{Q3} is

independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; and

 Y_1 and Y_2 are independently hydrogen, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or $-WR^{Y1}$; wherein W is independently -O-, -S- or $-NR^{Y2}$ -, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or Y_1 and Y_2 together with the carbon atom to which they are attached form a moiety having the structure:

whereby the composition is formulated for administration to a subject at a dosage between about 0.1 mg/kg to about 50 mg/kg of body weight.

- 2. The composition of claim 1, wherein the dosage is between about 1 mg/kg to about 50 mg/kg of body weight.
- 3. The composition of claim 1, wherein the dosage is between about 0.1 mg/kg to about 40 mg/kg of body weight.
- 4. The composition of claim 1, wherein the dosage is between about 1 mg/kg to about 40 mg/kg of body weight.
- 5. The composition of claim 1, wherein the dosage is between about 0.1 mg/kg to about 30 mg/kg of body weight.
- 6. The composition of claim 1, wherein the dosage is between about 5 mg/kg to about 30 mg/kg of body weight.
- 7. The composition of claim 1, wherein the dosage is between about 1 mg/kg to about 30 mg/kg of body weight.

- 8. The composition of claim 1, wherein the dosage is between about 0.1 mg/kg to about 20 mg/kg of body weight.
- 9. The composition of claim 1, wherein the dosage is between about 1 mg/kg to about 20 mg/kg of body weight.
- 10. The composition of claim 1, wherein the dosage is 10 mg/kg or greater of body weight.

11. The composition of claim 1, wherein:

 $\mathbf{R_1}$ and $\mathbf{R_2}$ are each independently hydrogen or substituted or unsubstituted lower alkyl; or $\mathbf{R_1}$ and $\mathbf{R_2}$, taken together with the carbon atoms to which they are attached, form an epoxide, an aziridine or a substituted or unsubstituted cyclopropyl moiety;

R₃ is hydrogen, or substituted or unsubstituted lower alkyl or aryl; a prodrug moiety or an oxygen protecting group;

 R_4 is halogen, $-OR^{4A}$, $-OC(=O)R^{4A}$ or $-NR^{4A}R^{4B}$; wherein R^{4A} and R^{4B} are independently hydrogen, or substituted or unsubstituted lower alkyl; a prodrug moiety, a nitrogen protecting group or an oxygen protecting group; or R^{4A} and R^{4B} , taken together with the nitrogen atom to which they are attached, form a heterocyclic or heteroaryl moiety; or R_4 , taken together with the carbon atom to

which it is attached forms a moiety having the structure: $V_{N}^{P^{1}} = N^{P^{1}} = N^$

 R_5 and R_6 are each independently hydrogen or substituted or unsubstituted lower alkyl; or R_6 and R_c , taken together with the carbon atoms to which they are attached, form an epoxide, an aziridine or a substituted or unsubstituted cyclopropyl moiety;

 R_a and each occurrence of R_b are independently hydrogen, halogen, alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety, or $-WR^{al}$; wherein W is independently -O-, -S- or -NR^{a3}-, wherein each occurrence of R^{al} , and R^{a3} is independently hydrogen, or an alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety; or R_a and the adjacent occurrence of R_b , taken together, form an epoxide, an aziridine or a substituted or unsubstituted cyclopropyl moiety;

 R_c is hydrogen, halogen, alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety, or $-WR^{c1}$; wherein W is independently -O-, -S- or $-NR^{c3}$ -, wherein each occurrence of R^{c1} and R^{c3} is independently hydrogen, or an alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety; or R_c and R_6 , taken together with the carbon atoms to which they are attached, form an epoxide, an aziridine or a substituted or unsubstituted cyclopropyl moiety;

n is an integer from 1 to 5;

 X_1 is O, S, NR^{X1} or $CR^{X1}R^{X2}$; wherein R^{X1} and R^{X2} are independently hydrogen, halogen, substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl, or a nitrogen protecting group;

Q is hydrogen, halogen, -CN, -S(O)₁₋₂R^{Q1}, -NO₂, -COR^{Q1}, -CO₂R^{Q1}, -NR^{Q1}C(=O)R^{Q2}, -NR^{Q1}C(=O)OR^{Q2}, -CONR^{Q1}R^{Q2}, an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or -WR^{Q1}; wherein W is independently -O-, -S- or -NR^{Q3}-, wherein each occurrence of R^{Q1}, R^{Q2} and R^{Q3} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety;

 Y_1 and Y_2 are independently hydrogen, an alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety; or $-WR^{Y1}$; wherein W is independently -O-, -S- or $-NR^{Y2}$ -, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or an alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety; or Y_1 and Y_2 together with the carbon atom to which they are attached form

a moiety having the structure:
$$v_{1}^{P} = 0$$
, $v_{2}^{P} = 0$, $v_{3}^{P} = 0$, $v_{4}^{P} = 0$, $v_{4}^{P} = 0$, $v_{5}^{P} = 0$, $v_{5}^{$

12. The composition of claim 1, wherein R_a , R_b and R_c are each hydrogen, and the compound has one of the following structures:

wherein R_1 - R_6 , Y_2 , X_1 , n and Q are as defined in claim 1; W is O or NH; and R^{Y1} is hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety.

13. The composition of claim 1, wherein R_a , R_b and R_c are each hydrogen, Q is a carbonyl-containing moiety and the compound has one of the following structures:

wherein R₁-R₆, Y₂, X₁, and n are as defined in claim 1; W is O or NH; and R^{Y1} is hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; R₇ is a substituted or unsubstituted lower alkyl or heteroalkyl moiety; R₈ is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety; and Alk is a substituted or unsubstituted C₀₋₆alkylidene or C₀₋₆alkenylidene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl.

14. The composition of claim 1, wherein R_a , R_b and R_c are each hydrogen, n is 3 and the compound has one of the following structures:

wherein R_1 - R_6 , Y_2 , Q and X_1 are as defined in claim 1; W is O or NH; and R^{Y1} is hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety.

15. The composition of claim 1, wherein R_a , R_b and R_c are each hydrogen, n is 3, Q is a carbonyl-containing moiety, and the compound has one of the following structures:

wherein R_1 - R_6 , X_1 and Y_2 are as defined in claim 1; W is O or NH; R^{Y1} is hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; R_7 is a substituted or unsubstituted lower alkyl or heteroalkyl moiety; R_8 is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl,

heterocycloalkyl, aryl or heteroaryl moiety; and Alk is a substituted or unsubstituted $C_{0.6}$ alkylidene or $C_{0.6}$ alkenylidene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; and R₈ is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety.

- 16. The composition of any one of claims 1 and 11-15, wherein R_1 and R_2 are each hydrogen.
- 17. The composition of any one of claims 1 and 11-15, wherein R_5 and R_6 are each methyl.
- 18. The composition of any one of claims 1 and 11-15, wherein R₃ is lower alkyl.
- 19. The composition of claim 18, wherein R_3 is methyl.
- 20. The composition of any one of claims 1 and 11-15, wherein R_4 is OH, NH_2 or halogen.
- 21. The composition of claim 13 or 15, wherein R₇ is lower alkyl.
- 22. The composition of claim 21, wherein R_7 is methyl.
- 23. The composition of any one of claims 1, 11-12 and 14, wherein Q has the structure:

wherein R₇ is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R₈ is a substituted or unsubstituted carbocyclic, heterocyclic, aryl or heteroaryl moiety; and X, Y and Z are independently a bond, - O-, -S-, -C(=O)-, -NR^{Z1}-, -CHOR^{Z1}, -CHNR^{Z1}R^{Z2}, C=S, C=N(R^{Y1}) or -CH(Hal); or a substituted or unsubstituted C₀₋₆alkylidene or C₀₋₆alkenylidene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein Hal is a halogen selected from F, Cl, Br and I; and each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; or R^{Z1} and R^{Z2}, taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety; and pharmaceutically acceptable derivatives thereof.

24. The composition of claim 23, wherein Q has the structure:

wherein R₇ is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R₈ is a substituted or unsubstituted carbocyclic, heterocyclic, aryl or heteroaryl moiety; and R^Y is hydrogen, halogen, -OR^{Y1} or -NR^{Y1}NR^{Y2}; wherein R^{Y1} and R^{Y2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y1} and R^{Y2}, taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

25. The composition of any one of claims 13, 15, 23 and 24, wherein R_8 is one of:

wherein p is an integer from 0 to 5; q is 1 or 2, r is an integer from 1 to 6; each occurrence of R^{8A} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, -OR^{8C}, -SR^{8C}, -N(R^{8C})₂, -SO₂N(R^{8C})₂, -(C=O)N(R^{8C})₂, halogen, -CN, -NO₂, -(C=O)OR^{8C}, -N(R^{8C})(C=O)R^{8D}, wherein each occcurrence of R^{8C} and R^{8D} is independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl; and each occurrence of R^{8B} is independently hydrogen or lower alkyl.

26. The composition of claim 25, wherein R₈ has the structure:

wherein R8B is hydrogen or lower alkyl.

- 27. The composition of claim 1, 11, 12 or 13, wherein n is 3.
- 28. The composition of claim 12, 13, 14 or 15, wherein Y_1 is OR^{Y_1} and Y_2 is lower alkyl; wherein R^{Y_1} is hydrogen or lower alkyl.

- 29. The composition of claim 28, wherein Y_1 is OH and Y_2 is CF_3 .
- 30. The composition of claim 11 wherein R_a , R_b and R_c are each hydrogen, and the compound has one of the structures:

or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 , n and Q are as defined in claim 1; and Y_2 and R^{Y1} are independently hydrogen or lower alkyl.

or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 and Q are as defined in claim 11; and Y_2 and R^{Y1} are independently hydrogen or lower alkyl.

or pharmaceutically acceptable derivative thereof;

wherein R₃-R₆ and n are as defined in claim 11; Y₂ and R^{Y1} are independently hydrogen or lower alkyl; R₇ is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and X, Y and Z are independently a bond, -O-, -S-, -C(=O)-, -NR^{Z1}-, -CHOR^{Z1}, -CHNR^{Z1}R^{Z2}, C=S, C=N(R^{Y1}) or -CH(Hal); or a substituted or unsubstituted C₀. 6alkylidene or C₀-6alkenylidene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein Hal is a halogen selected from F, Cl, Br and I; and each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; or R^{Z1} and R^{Z2}, taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

33. The composition of claim 11 wherein the compound has the structure:

or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and X, Y and Z

are independently a bond, -O-, -S-, -C(=O)-, -NR^{Z1}-, -CHOR^{Z1}, -CHNR^{Z1}R^{Z2}, C=S, C=N(R^{Y1}) or -CH(Hal); or a substituted or unsubstituted C₀₋₆alkylidene or C₀₋₆alkenylidene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein Hal is a halogen selected from F, Cl, Br and I; and each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; or R^{Z1} and R^{Z2}, taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

- 34. The composition of claim 32 or 33, wherein -X-Y-Z together represents the moiety $-CH_2-Y-CH_2-$; wherein Y is $-CHOR^{Y1}$, $-CHNR^{Y1}R^{Y2}$, C=O, C=S, C=N(R^{Y1}) or -CH(Hal); wherein Hal is a halogen selected from F, Cl, Br and I; and R^{Y1} and R^{Y2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y1} and R^{Y2} , taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.
- 35. The composition of claim 11 wherein the compound has the structure:

wherein R₃-R₆ and n are as defined in claim 11; Y₂ and R^{Y1} are independently hydrogen or lower alkyl; R₇ is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and Y is -CHOR^{Y1}, -CHNR^{Y1}R^{Y2}, C=O, C=S, C=N(R^{Y1}) or -CH(Hal); wherein Hal is a halogen selected from F, Cl, Br and I; and R^{Y1} and R^{Y2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y1} and R^{Y2}, taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

wherein R_3 - R_6 are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and Y is – CHOR^{Y1}, -CHNR^{Y1}R^{Y2}, C=O, C=S, C=N(R^{Y1}) or -CH(Hal); wherein Hal is a halogen selected from F, Cl, Br and I; and R^{Y1} and R^{Y2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y1} and R^{Y2} , taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

wherein n, R_3 and R_4 are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R^{8B} is hydrogen or lower alkyl; and R^Y is hydrogen, halogen, $-OR^{Y1}$ or $-NR^{Y1}NR^{Y2}$; wherein R^{Y1} and R^{Y2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y1} and R^{Y2} , taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

wherein R_3 and R_4 are as defined in claim 11; Y_2 and R^{Y_1} are independently hydrogen or lower alkyl; R^{8B} is hydrogen or lower alkyl; and R^Y is hydrogen, halogen, $-OR^{Y_1}$ or $-NR^{Y_1}NR^{Y_2}$; wherein R^{Y_1} and R^{Y_2} are independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl, or R^{Y_1} and R^{Y_2} , taken together with the nitrogen atom to which they are attached, for a heterocyclic or heteroaryl moiety.

39. The composition of claim 11 wherein the compound has the structure:

wherein R_3 - R_6 and n are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; and R^{8B} is hydrogen or lower alkyl.

wherein R_3 - R_6 are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, linear or branched, cyclic or acyclic lower alkyl moiety; and R^{8B} is hydrogen or lower alkyl.

or a pharmaceutically acceptable salt thereof; wherein X_1 is CH_2 , NH or O;

 Y_1 and Y_2 are independently OH, $C(R^{Y1})_3$ or Y_1 and Y_2 taken together with the carbon atom to which they are attached are -C=0, wherein R^{Y1} is halo;

R₆ is H or lower alkyl; R₅ is H or lower alkyl; R₄ is OH; and R₃ is alkyl.

42. The composition of claim 41 wherein the compound has one of the following structures:

- 43. The composition of claim 1, wherein the compound is present in an amount effective to inhibit metastasis of tumor cells.
- 44. The composition of claim 1, wherein the compound is present in an amount effective to inhibit angiogenesis.
- 45. The composition of claim 1, further comprising a cytotoxic agent.
- 46. The composition of claim 45, wherein the cytotoxic agent is an anticancer agent.
- 47. The composition of claim 1, further comprising a palliative agent.
- 48. A method for treating breast tumor metastasis in a subject comprising: administering to a subject in need thereof a therapeutically effective amount of the composition of claim 1.
- 49. The method of claim 48, wherein the dosage is between about 1 mg/kg to about 50 mg/kg of body weight.
- 50. The method of claim 48, wherein the dosage is between about 0.1 mg/kg to about 40 mg/kg of body weight.
- 51. The method of claim 48, wherein the dosage is between about 1 mg/kg to about 40 mg/kg of body weight.
- 52. The method of claim 48, wherein the dosage is between about 0.1 mg/kg to about 30 mg/kg of body weight.
- 53. The method of claim 48, wherein the dosage is between about 1 mg/kg to about 30 mg/kg of body weight.

- 54. The method of claim 48, wherein the dosage is between about 5 mg/kg to about 30 mg/kg of body weight.
- 55. The method of claim 48, wherein the dosage is between about 0.1 mg/kg to about 20 mg/kg of body weight.
- 56. The method of claim 48, wherein the dosage is between about 1 mg/kg to about 20 mg/kg of body weight.
- 57. The method of claim 48, wherein the dosage is 10 mg/kg or greater of body weight.
- 58. The method of claim 48 wherein in the composition, the compound has one of the following structures:

- 59. The method of claim 58, wherein the composition is administered at a dosage between about 10 mg/kg to about 20 mg/kg of body weight.
- 60. The method of claim 48, further comprising administering a cytotoxic agent.
- 61. The method of claim 60, wherein the cytotoxic agent is an anticancer agent.
- 62. The method of claim 48, further comprising administering a palliative agent.